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Letters to the Editor

Oscillatory neural activity of anteromedial globus pallidus internus in Tourette syndrome

Empirical data to support the use of deep brain stimulation (DBS) as a treatment for refractory Tourette syndrome (TS) is increasing (Saleh et al., 2012). Several clinical case series have been published, but few studies have examined the electrophysiology of the DBS target nuclei. We present the first electrophysiological description of simultaneously recorded single units and local field potentials (LFPs) from anteromedial globus pallidus (GPi) in TS patients.

The electrophysiological characteristics of the posterolateral GPi have been well described in Parkinson's disease (PD) and dystonia. However, no data exist on GPi neural activity in TS. One prior study of thalamic neural activity in TS described oscillatory activity at low frequencies (2–7 Hz) and alpha band, but no beta-band activity (Marceglia et al., 2010). Although there is no consensus as to the best target nucleus for TS, we targeted the anteromedial GPi based on recently published efficacy reports (Welter et al., 2008; Martínez-Fernández et al., 2011).

Patient 1 is a 41 year-old man with vocal, motor, and self-injurious tics. Patient 2 is a 43 year-old man with frequent self-injurious tics that led to enucleation. Both patients had TS diagnosed in childhood and were refractory to medicines. DBS electrodes (Medtronic Model 3387) were implanted into the bilateral anteromedial GPi, under isoflurane anesthesia. Implantation location was confirmed by postoperative CT in patient 1 and by MRI in patient 2. Patient 1 had a post-operative reduction in tic severity from 83 to 11 on the Yale Global Tic Severity Scale (YGTSS), and from 13 to 5 on the Modified Rush Tic Rating scale (MRTRS). Patient 2 had tic severity reduction from 82 to 44 (YGTSS) and from 14 to 8 (MRTRS). Current DBS settings and post-op coordinates are as follows: patient 1: left C+0−, 3.9 V, right C+8−, 4.9 V, pulse width (PW) 60 μs, rate 130 Hz, left: X −12.3, Y 9.75, Z −4, right: X 12.2, Y 9.75, Z −3; patient 2: left C+1−, right C+9−, 2.8 V, PW 90 μs, rate 160 Hz, left: X −11.2, Y 10, Z −5, right: X 11.7, Y 10, Z −4.

Seventeen episodes (94.6 ± 67.5 s) of neuronal units and LFPs were recorded from the anteromedial GPi during microelectrode-guided targeting using the FHC Guideline 4000 modified to record *both* neuronal units and LFPs. Hardware filtering of spikes and LFP and subsequent off-line analysis (spike extraction and sorting and spectral analysis performed in MATLAB) have being described in application to parkinsonian data (Park et al., 2010). The fast Fourier transform of individual epochs was squared and then averaged, yielding the power spectral estimate. An uncorrected Welch's power spectral density (PSD) estimate was normalized by the maximum of PSD. Magnitude squared coherence (MSC) between spikes and LFP was computed using Welch's averaged, modified periodogram method. Confidence levels of PSD and MSC were computed under the assumptions of random sample and independence, respectively.

Experimental data analysis revealed the presence of statistically significant oscillatory activity in low frequencies (2–3 Hz) and alpha and beta bands (see Fig. 1, upper panel). While the two patients do not have identical power spectra, the activity in both alpha and beta bands is visible in some episodes for each patient. These differences may be due to different constellations of symptoms or different actions of anesthesia. Larger difference in mean power spectra and more similarity between spectra of several recording episodes may be due to differences in the locations of the recording electrode during some recorded episodes. The lower panels in Fig. 1 show that the coherence between spikes and LFP for each patient was below the 95% confidence level at all frequency ranges for both patients. Thus the synchrony between spikes and LFPs is very low.

Our observations of low frequency and alpha band activity in the GPi are consistent with prior findings from the thalamus in TS (Marceglia et al., 2010). This may suggest that low frequency and alpha oscillations may be a feature of hyperkinetic movement disorders like TS. This is in contrast to hypokinetic disorders, which are characterized by prominent beta oscillations expressed throughout cortico-subcortical loops, including the thalamus. The similarity of our observations with thalamic oscillatory neural activity in the same frequency band may suggest that the basal ganglia and thalamic territories are engaged in the same functional brain networks in TS. This may be similar to PD, where pathological oscillations in basal ganglia-thalamocortical circuits were implied to be related to motor symptoms.

In contrast to findings from the thalamus (Marceglia et al., 2010), we observed beta band activity in our GPi recordings, which may suggest that the GPi in TS is engaged in other types of neural activities; and that the relationship between beta band activity and hyperkinetic behavior may be complicated. Lastly, because LFP is thought to be primarily generated by synaptic activity, low synchrony between spikes and LFPs may suggest that the pallidum, in TS, possibly fails to form appropriate neural assemblies to inhibit appropriate motor programs. This is in contrast to the synchrony between spikes and LFPs in PD, which is thought to be responsible for generating the hypokinetic features of PD.

One limitation of this study is that recordings were performed while patients were under general anesthesia. However, Marceglia et al. (2010) found similar results in the thalamus when recording awake postoperative LFPs. Further, they found that the interburst frequency (recorded intraoperatively under anesthesia) was similar to the frequency of LFP oscillations (recorded postoperatively without anesthesia). Similarly, in our case the effect of anesthesia on the rhythmicity may be limited.

The precise understanding of the pathophysiological basis of TS is still elusive. While this report is limited by small sample size, it is the first description of neuronal oscillatory activity in the GPi. Improved understanding of abnormal brain activity in TS is essential for future therapy development.

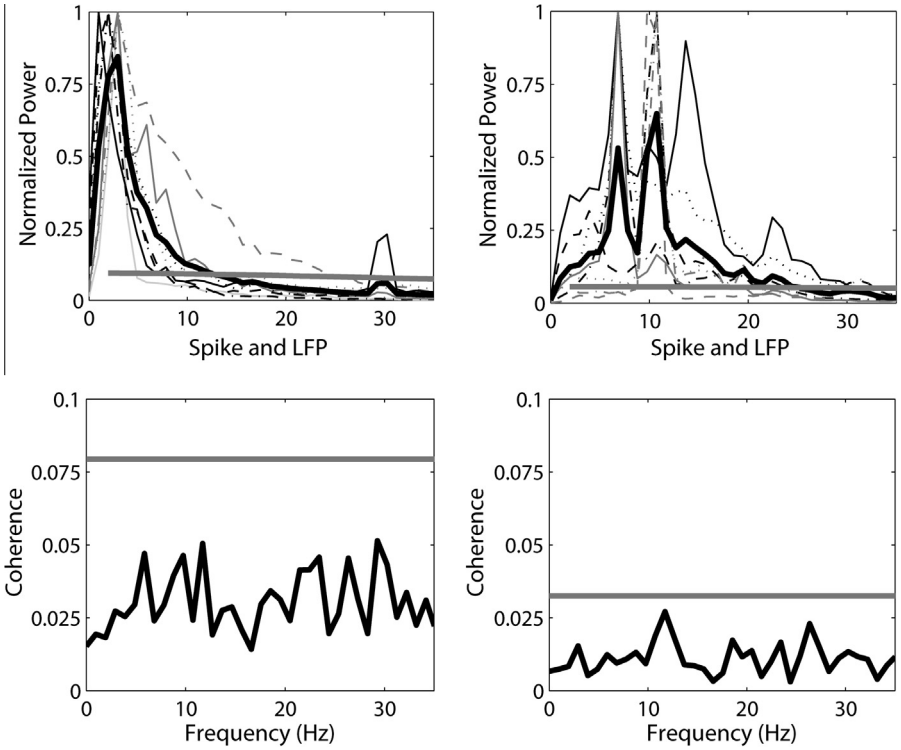

Fig. 1. Normalized PSDs of LFPs (upper row) and mean MSCs for single unit-LFP (lower row). Thick black lines are the mean values and thick gray lines are 95% upper confidence levels.

Ethics statement

This research was conducted in compliance with the Declaration of Helsinki and was approved by Indiana University IRB. The authors have no conflict of interest.

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